external medium, and diffusional release starts immediately. After some time a steady-state rate of diffusional release is established. At this stage, two 'concentration layers' exist within the tip of the micropipette: (1) the bulk of the drug solution, where the concentration of drug molecules is uniform, (2) an interphase layer, where the concentration gradually decreases towards the external medium (Ficks first law of diffusion).

When a retaining potential is applied to the drug solution, the drug ions drift away from the tip of the micropipette. This drift is not opposed by diffusion in the bulk of the solution, whereas in the interphase layer the net ion movement is the difference between the inward iontophoretic and outward diffusional ion fluxes. If the iontophoretic flux (R_i) is smaller than the diffusional flux (R_D), the retaining potential cannot counteract diffusional drug release instantaneously. However, the iontophoretic flux in the bulk of the solution gradually increases the thickness of the interphase layer, thus reducing the concentration gradient. Consequently, the rate of diffusional ion transport declines until $R_i = R_D$, and there is no diffusional release. Thus a retaining current, which initially is not adequate, can after some time ('minimal effective retention time') become effective. If a retaining current is applied longer than the minimal effective retention time, the whole interphase layer moves away from the tip, and the terminal part of the micropipette becomes depleted of drug ions.

When an ejected potential is applied, after a period of drug retention, the onset of release may be delayed ('release latency'), and it may take some time before a steady-state rate of release is established. The release latency corresponds to the time which is necessary for the interphase layer to reach the tip orifice, and the establishment of the steady-state rate of release reflects the arrival of the bulk of the solution at the tip orifice.

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The effect of anti-Parkinson drugs on catalepsy induced by α-methyl-*p*-tyrosine in rats pretreated with intraventricular 6-hydroxydopamine

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Catalepsy may be induced in rats by agents which impair dopaminergic function, such as reserpine or haloperidol. Surprisingly, α-methyl-*p*-tyrosine (αMPT), 250 mg/kg I.P., a specific inhibitor of catecholamine biosynthesis produces only a marginal catalepsy. Recently, Sayers & Spencer (1971) reported that high doses of dexamphetamine caused marked catalepsy in rats pretreated with αMPT. The effect was not attributed to depletion of dopamine (DA) since Corrodi, Fuxe & Hökfelt (1967) have shown brain DA concentrations to be little affected by dexamphetamine in αMPT pretreated rats. However, noradrenaline (NA) is reduced by dexamphetamine at high doses indicating that reduced NA may be a prerequisite for the induction of catalepsy with αMPT. In order to investigate this hypothesis we have selectively reduced brain NA in rats by the intraventricular injection of 6-hydroxydopamine (6-OHDA) (250 μg base). When αMPT (250 mg/kg I.P.) is given to these rats 10 to 15 days after 6-OHDA a marked catalepsy occurs, commencing about 4 h after dosing and lasting for over 24 h, during which time NA stores would be low and DA synthesis inhibited.

We have used the reversal of this long lasting catalepsy to characterize the action of a range of drugs, active in Parkinsonism and/or reserpine induced catalepsy in rats. Drugs were given 18 h after αMPT and catalepsy scored at half-hourly intervals for 4·5 h using the method described by Simon, Malatroy & Boissier (1970). Catalepsy was inhibited by amantadine (40 mg/kg S.C.), apomorphine (2·5 mg/kg S.C.), benztropine

(20 mg/kg S.C.), hyoscine (2·5 mg/kg S.C.) and L-DOPA (100 mg/kg P.O., given with the peripheral DOPA decarboxylase inhibitor, Ro-4-4602, 50 mg/kg I.P.). Dexamphetamine (10 mg/kg S.C.), L-amphetamine (20 mg/kg S.C.) and methylphenidate (20 mg/kg P.O.) have no significant effect.

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A modified motor activity test to discriminate major and minor tranquillizers

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In the screening for major and minor tranquillizers there is no single test sufficiently sensitive and flexible to distinguish between classes of tranquillizing agents, or having the potential to recognize a novel type of activity (Irwin, 1962). The test we have evaluated could well possess some of these attributes. Its presentation here is primarily to introduce its potential discriminative powers for different classes of sedative and tranquillizing compounds. The test design is a modification of Somers' motor activity experiment where animals are dosed and 30 min later placed in a 'Perspex' motor activity counting chamber and their perambulatory activity recorded every 5 min over a 1 h period. Upon this is imposed a facility so that the animals may be submitted to photic stimuli at regular time intervals throughout the test period.

This intermittent photic stimulus caused an increase in the overall activity of the control animals and a change in their pattern of behaviour over the 1 h period. Dosed animals showed different patterns of behaviour which were related to the type of drug adopted, and the effects were reproducible.

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Analysis of labile brain constituents using a technique for the instantaneous fixation of brain tissue *in vivo*

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It is well established that, in order to preserve the *in vivo* levels of many metabolites in the central nervous system, it is essential to stop metabolism as quickly as possible by means of rapid freezing. The procedure most commonly used for small animals is the total immersion of the whole animal in a liquid gas or in fluorocarbons cooled to their freezing point with liquid nitrogen. Since these techniques take several seconds to freeze the innermost regions of the brains of rats and mice (Ferrendelli, Gay, Sedgwick & Chang, 1972) it is likely that post-mortem alterations in brain metabolites are unavoidable even under these conditions.

A new apparatus has recently been devised (Veech, Harris, Veloso & Veech, 1972) with which it is possible to remove and fix brain tissue in less than one second. The forebrain of rats or mice is instantaneously expelled under pressure on to an aluminium disc previously cooled in liquid nitrogen. Using such a machine, we have confirmed the